



Primary Pulmonary Ewing's Sarcoma / Primitive Neuroectodermal Tumor (ES/PNET) Case

Primer Pulmoner Ewing Sarkomu / Primitif Nöroektodermal Tümör (ES/PNET) Olgusu

ES/PNET of Lung

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Özet

Ewing Sarkomu /Primitif Nöroektodermal Tümörler (ES/PNET) çocuk ve adolesanlarda osteosarkomdan sonra görülen 2. en sık primer malign kemik tümörleridir. Genellikle ekstremitelerin uzun kemiklerinde görülürler. Primer pulmoner ES/PNET çok nadirdir ve literatürde sadece olgu sunumları şeklinde bildirilmiştir. 24 yaşındaki erkek hastamızın bilateral multipl pulmoner kitle ve nodülü mevcuttu ve yapılan transtorasik biyopsi sonucu ES/PNET olarak değerlendirildi. Pozitron Emisyon Tomografi/Bilgisayarlı Tomografi ve tüm vücut kemik sintigrafisi ile vücudunun başka bir alanında primer odak saptanmayan olgumuz primer pulmoner ES/PNET' in, bilateral multipl pulmoner metastazı olarak kabul edildi. Bugüne kadar literatürde sadece yirmi primer pulmoner ES/PNET olgusu ve iki tane pulmoner metastaz olgusu bildirilmiştir. Bu olgu primer pulmoner ES/PNET'in bilateral multipl pulmoner metastazla seyreden üçüncü olgusu olması nedeni ile sunulmuştur.

Anahtar Kelimeler

Ewing Sarkomu; Primitif Nöroektodermal Tümör; Multipl Pulmoner Nodüller

Abstract

Ewing Sarcoma/Primitive neuroectodermal tumor (ES/PNET) is the second most common primary malignant bone tumor, following osteosarcoma, in children and adolescents, most often arising in long bones. Primary pulmonary ES/PNET is very rare and is seen only as case reports in the literature. Here, we report on a 24-year-old man who had bilateral multiple pulmonary masses and nodules on a chest X-ray. By transthoracic biopsy he was diagnosed with ES/PNET. Since no other primary focus was determined in his Positron Emission Tomography-Computed Tomography and total body bone scan, the patient was accepted as primary pulmonary ES/PNET. To our knowledge only twenty cases have been described in the English literature and of them only two had intrapulmonary multiple metastases. We present this case because he will be the third reported ES/PNET case which has been seen with bilateral multiple pulmonary metastases.

Keywords

Ewing's Sarcoma, PNET, Multiple Pulmonary Nodules

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Introduction

Histologically, ES/PNET consists of malignant small round cell tumors previously regarded as different entities. Recent immunohistochemical and cytogenetic studies indicate that they are the same entity with varying degrees of neuroectodermal differentiation. ES/PNET typically arises from the skeletal system and soft tissues; on rare occasions it is reported in other sites, such as the uterus, ovary, kidney, pancreas, palate, testis, colon, myocardium, and lung [1]. PNETs that arise in the lung parenchyma without pleural or chest wall involvement are exceptionally rare. Here we present our extremely rare case of primary pulmonary ES/PNET with bilateral multiple pulmonary masses.

Case Report

A 24-year-old man was admitted to a regional hospital with cough and chest pain. Since his chest X-ray revealed multiple masses and nodules, he was sent to our hospital for further evaluation. He was an active smoker and working as a tire repair person. The chest X-ray revealed multiple masses and bilateral nodules. A thoracic computed tomography (CT) scan showed multiple well-defined nodules and mass images bilaterally, the largest of which was 9 cm in diameter located in the right upper lobe (Figure 1). Bronchoscopy revealed no abnormal

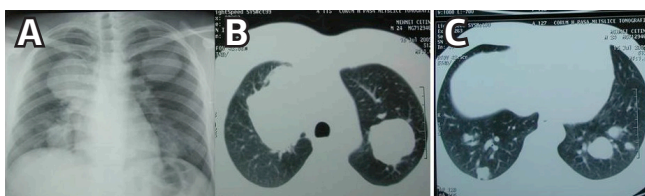


Figure 1. The chest X-ray revealed multiple masses and bilateral nodules.

findings. His tumor markers including CEA, CA 19-9, total PSA and free PSA and scrotal ultrasonographic findings were also normal. The F-18 Fluoro-2-deoxy-D-glucose Positron Emission Tomography (FDG-PET) scan revealed multiple, lobulated, well-defined masses and nodules, the largest of which was 7x6, 8x8, 4 cm in the right upper lobe and extending towards the middle lobe with a high metabolic activity rate (maximum standardized uptake value (SUVmax):11,75). At the left side a 5.5x5, 4x5, 5cm mass was presented and the SUVmax was 8.61. There were no abnormal hypermetabolic lesions at any other sites (Figure 2). The fiberoptic bronchoscopy was normal. The CT-guided

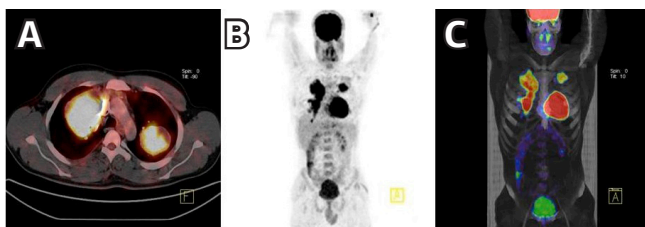


Figure 2. FDG-PET scan revealed multiple, lobulated, well-defined masses and nodules with a high metabolic activity. PET-CT scan showed no evidence of any other primary foci or distant metastases.

transthoracic needle biopsy was performed from the left site. Hematoxylin-eosin (H&E) stained tissue sections showed small atypical neoplastic cells with small round nuclei and scanty eosinophilic cytoplasm. These cells were stained positive by PAS. Immunohistochemical stains were positive for CD99 diffusely (strong membranous MIC-2 immunoreactivity), and for CD56

focally (Figure 3). To exclude other small cell tumors, markers

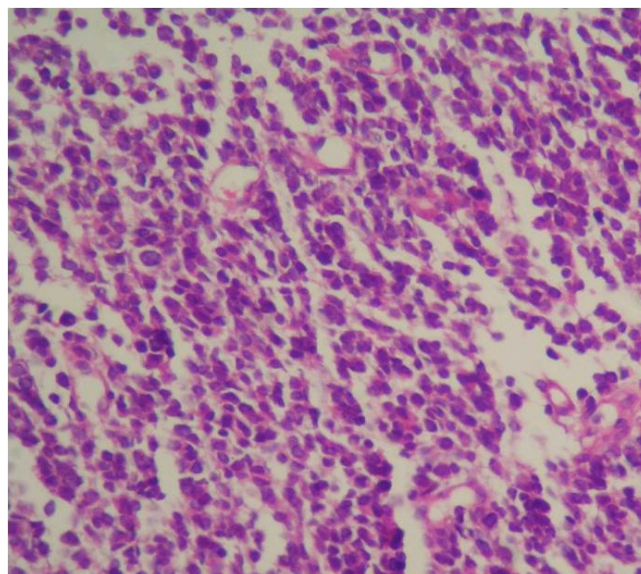


Figure 3. Hematoxylin-eosin (H&E) stained tissue sections showed small atypical neoplastic cells with small round nuclei and scanty eosinophilic cytoplasm. These cells were stained positive by PAS; also, CD99 diffusely and CD56 focally were positive.

including thyroid transcription factor 1 (TTF-1), pancytokeratin, and chromogranin were studied and all were found negative. The histological and immunohistochemical findings were compatible with ES/PNET. The patient underwent a whole body technetium bone scan and cranial CT to estimate the possible primary focus. But there was no evidence of any other primary foci or distant metastases. As a result we have diagnosed the patient as primary pulmonary ES/PNET with multiple pulmonary masses bilaterally. The patient was referred to the medical oncology department for follow-up and treatment. He had six courses of chemotherapy with vincristine, adriamycin, and cyclophosphamide. At the end of the chemotherapy the size of the nodules had decreased.

Discussion

ES and extraskeletal ES have been confused histologically with other small cell tumors including PNET. After development of new immunohistochemical and cytogenetic techniques, PNET and ES were accepted as the same entities with different degrees of neuroectodermal differentiation and subsequently were classified in a group known as Ewing's Sarcoma Family Tumors (ESFT) [2].

ES/PNET tumors mostly arise in the bones and soft tissue; however, they occasionally originate from the ovaries, uterus, kidney, pancreas, colon, hard palate, and lung. Primary pulmonary ES/PNET is very rare. Takahashi et al. found only eight cases in their literature review of 2006 [1]. We have discovered eleven primary pulmonary ES/PNET cases which were not presented in that study. When we review the total of twenty primary pulmonary ES/PNET cases (one of which belongs to us), thirteen of the patients were male and the median age was 30 (between 8 and 67) years. Only six out of twenty cases were in the childhood and adolescent period (between 2 and 13 years old). Five of the patients in this small sample had no symptoms at the time of administration and their radiologic images were found incidentally while four of the others presented with hemoptysis.

Others had symptoms of chest pain, fever, cough, or dyspnea. Lesion sizes range from 4cm to 16cm. The most common CT finding of ES/PNET was a heterogeneously enhancing mass with an occasional central, nonenhancing low density area suggesting necrosis or hemorrhage. Of the cases who had FDG-PET scans, the SUVmax values were between 6.22 and 13.9 [2-5]. Our patient had cough and chest pain when he was admitted to the hospital. Of his multiple nodules and masses, the largest one was 7x6.8x8.4 cm in size with a SUVmax of 11.75.

Morphologically, ES/PNET is generally composed of sheets and cords of closely located uniform small round cells with scanty cytoplasm and indistinct cytoplasmic membranes. The cytoplasm of the tumor cells frequently contains PAS positive glycogen [6]. PAS (+) tumor cells and CD99 expression is helpful in the histologic differential diagnosis of the ES/PNET from other small, round cell tumors such as malignant lymphoma, embryonal rhabdomyosarcoma and neuroblastoma. In our case, immunohistochemically CD99 was diffusely expressed in the cell surface membranes and histologically cells were stained with PAS. Both these findings were compatible with ES/PNET.

Due to the limited number of cases of ES/PNET, the optimal treatment is unknown. Previously reported primary pulmonary ES/PNET cases were treated with different combinations of surgery, chemotherapy, and radiation therapy. The follow-up period was between three months to four years. Generally patients with metastases at the time of diagnosis have a five-year survival rate of 20-30% [1]. Since he had bilateral multiple pulmonary masses and nodules, our patient had six courses of chemotherapy with vincristine, adriamycin, and cyclophosphamide. At the end of one year, the nodule size was decreased.

In conclusion, primary pulmonary ES/PNET is a very rare tumor, and bilateral multiple intrapulmonary metastases is an extremely rare manifestation of this disease. To date in the English literature, of twenty previously reported cases, only two had pulmonary metastases [7, 8]. This is the third report of primary pulmonary ES/PNET with bilateral multiple intrapulmonary metastases without pleural or chest wall involvement.

Competing interests

The authors declare that they have no competing interests.

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